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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,185	12/26/2000	Gilles Philippus van Wezel	4666US	6157

7590 08/07/2003

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/749,185	VAN WEZEL ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,11,13-19 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,11,13-19 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1, 3-9, 11, 13-19, 29-34 are currently pending and under consideration in this application.

Applicants' amendments and arguments filed on 5-27-03, paper No.14, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 29-34 and claims 3-9, 11, 13-19 all of which depend from claims 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 29-34 recite the phrase endogenous SsgA. It is not clear to the Examiner as to what applicants mean by "SsgA" in the context of the above claim.

Claims 1, 3-9, 11, 13-19, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, 4-7 and 29 recite the term "gene". The metes and bounds of this word is not clear to the Examiner. The word "gene" is understood n the art to be comprising more than just the cDNA sequence. A gene normally comprises the regulatory sequences, intron sequences (in eukaryotes) and the untranslated sequences. Therefore, it is not

clear to the Examiner as to whether applicants intend to include all those sequences or limit the sequences to only the cDNA. From claim 1 it appears that applicants are intending to use the cDNA for the purpose of transformation. Examiner suggests deletion of the above term and replace it "polynucleotide".

Claims 1, 29-34 and claims 3-9, 11, 13-19 all of which depend from claims 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "providing.....with the capability of having or expressing heterologous SsgA". The metes and bound of the above phrase is not clear to the Examiner. It appears that applicants are claiming a method to make a recombinant bacterium by either transforming or transfecting a bacterium with a heterologous polynucleotide encoding SsgA. Furthermore, while applicants give an example of a SsgA encoding polynucleotide from *S.griseus*, it is not clear whether that is in fact the polynucleotide used for transforming or making a recombinant bacterial cell. Applicants simply appear to be providing an example of the species of the genus but do not make it clear that it was SEQ ID NO:1 that they used.

Claims 5-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5-7 recite the phrase " of actinomycete origin" "of a streptomycete origin", "of Streptomyces.... origin" respectively. The metes and bounds of these phrases are not clear to the Examiner. Literally, while the term "origin" means "a source", the above term is

also synonymous to "derivation" that could also mean "to arrive at by reasoning i.e., to deduce or infer" or also mean "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. For example, it is not clear to the Examiner whether the "of actinomycete origin" encompasses specific cDNAs of an actinomycete or streptomycete or whether it encompasses recombinants, variants and mutants of any ssgA cDNA of any other source and labeled as "of actinomycete origin". As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean, that a "of actinomycete origin" and of actinomycete origin encompasses nucleic acid sequences which are recombinants, variants, or mutants of any cDNA. Examiner has given the same interpretation while considering the claims for all other rejections.

In response to the previous rejection, applicants have amended the claim with a synonymous term for derived which continuous to render the claims indefinite. Examiner suggests the use of the phrase "isolated from" in place of the above phrases.

Claims 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30-32 recites the phrase "means for enhancing". The metes and bounds of the above phrase is not clear to the Examiner. It is also not clear to the examiner as to what applicants mean by the above phrase in the context of the above claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 11, 13-19, 29, 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a filamentous *Streptomyces* bacterium exhibiting reduced branching and fragment septation and enhanced fragmentation using DNA with SEQ ID NO:1, does not reasonably provide enablement for such a method for rendering any or all filamentous actinomycete bacteria to exhibit reduced branching and fragment septation and enhanced fragmentation using DNA with SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 3-9, 11, 13-19, 29, 33 are so broad as to encompass methods for rendering any or all filamentous actinomycete bacteria to exhibit reduced branching and fragment septation and enhanced fragmentation using DNA with SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

Applicants have proposed the use the above polynucleotides for rendering any or all filamentous actinomycete bacteria to exhibit reduced branching and fragment septation and enhanced fragmentation using DNA with SEQ ID NO:1. However, applicants have not shown that their method will work for any or all filamentous actinomycete bacteria. Filamentous actinomycete bacteria are a large group of microorganisms and the method developed specifically for rendering *Streptomyces* sp. using a polynucleotide isolated from a *Streptomyces* sp. is not guaranteed to work in all types of actinomycetes. Furthermore, applicants have not shown that their method would work with any or all filamentous actinomycete bacteria. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein in the specific type of bacterium and thereby the phenotype of the transformant and since not all nucleic acids will have the same effect in any or all types of filamentous actinomycete bacteria, the method proposed by the applicants may not lead to desired function of the polynucleotides. This is because use of a *Streptomyces* polynucleotide exclusively shown to function in a *Streptomyces* sp. may not demonstrate the same effect in all or any type of filamentous actinomycete bacteria. However, in this case the disclosure is limited to the use of nucleotide sequence with SEQ ID NO:1 only in a *Streptomyces*.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass method of modifying all or any filamentous actinomycete bacteria because the specification does not establish: (A)that the proposed method will work in any or all types of filamentous actinomycete bacteria; (B) the general tolerance of all or any filamentous actinomycete bacteria to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any filamentous actinomycete bacteria with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all filamentous actinomycete bacteria in the above method. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, use of the above method against any or all filamentous bacteria is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have amended the claims and traversed the rejection arguing that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim then enablement requirement is satisfied. Applicants also argue that they have

provided working examples including *S.coelicolor*, *S.lividans*, *S.clavuligerus* and *Sacch.erhthraea* and since they have shown that the invention is enabled in four different actinomycetes the claim should be enabled. Examiner respectfully disagrees with the applicants that such an argument is persuasive to overcome the above rejection. This is because the family "Actinomycetes" is not limited to just *Streptomyces* and *Saccharothrix*. The family includes many more members of species and applicants have demonstrated in just two members. Furthermore, even though applicants have argued that they have shown enablement in four different actinomycetes, Examiner would like to point out that three of them belong to same genus, *Streptomyces*. Therefore, the above examples does not constitute four different actinomycetes. Therefore without guidance one of ordinary skill would be reduced to the necessity of producing and testing virtually large number of bacterial strains. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A)that the proposed method will work in any or all types of filamentous actinomycete bacteria; (B) the general tolerance of all or any filamentous actinomycete bacteria to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any filamentous actinomycete bacteria with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Claims 1, 3-9, 11, 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using the polynucleotide with SEQ ID NO:1 encoding a polypeptide with SEQ ID NO:3, to transform or transfect a filamentous bacteria, does not reasonably provide enablement for any DNA comprising ssgA gene, a derivative or fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 3-9, 11, 13-19 are so broad as to encompass any DNA with ssgA activity isolated from any source or derived from any source including derivatives, variants, mutants and recombinants. Examiner refers to his interpretation of the term derived from to the rejection under 35 U.S.C. 112 2nd paragraph. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

Applicants propose to use the above polynucleotides for the process of making transformants with a specific phenotypical characteristic. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and thereby the

phenotype of the transformant and since only nucleic acids with very high percent homology can be used for such purposes, changing the nucleotide sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:1 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that may or may not have the desired function. However, in this case the disclosure is limited to the single nucleotide sequence with SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA from any source because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of ssgA DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any DNA with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA or its derivative or fragment as having the above property. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 3-9, 11, 13-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a method of producing a filamentous bacterium using a genus of polynucleotides that have not been described in the specification.

The specification does not contain any disclosure of the structure of all such polynucleotides or genes comprising SsgA DNA sequences. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species, i.e., SEQ ID NO:1 of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one

skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-9, 11, 13-15, 29-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamoto et al. (Microbiology, April 1997, Vol. 143:1077-1086, listed by the applicant in the IDS, also see DNA and amino acid sequence alignment with database GenEmbl Accession No. D50051 and SPTREMBL_19, Accession No. P95753, May 1, 1997). This rejection is based upon the public availability of a printed publication one year before the effective filing date of the instant application. Claims 1, 3-9, 11, 13-15, 29-34 of the instant application are drawn to a method for producing a filamentous bacterium exhibiting reduced branching and fragment septation during growth or exhibiting enhanced fragmentation during growth, wherein the method comprises transforming a filamentous bacterium which lacks significant endogenous SsgA activity with a polynucleotide expressing SsgA activity and the sequence shown in SEQ ID NO:1, wherein the ssgA polynucleotide is derived from an actinomycete such as *S.griseus* etc., and wherein the polynucleotide is integrated into the bacterial genome or is a part of an episomal

element, wherein the ssgA activity is inducible or repressible with a signal, wherein the filamentous bacterium is an actinomycete such as *Streptomyces* and wherein the filamentous bacterium produces a useful product such as an antibiotic.

Kawamoto et al. disclose an identical method using a polynucleotide which is 100% identical to SEQ ID NO:1, isolated from *S.griseus*, which when transformed into another actinomycete lacking detectable endogenous SsgA such as Strain NRRL B2682, results in formation of septate form of the bacterium, wherein the polynucleotide is integrated into the genome or resides as an episomal element, wherein the expression of the gene product is inducible and wherein the actinomycete bacterium produces a useful product such as an antibiotic, streptomycin and wherein the polynucleotide encodes a polypeptide comprising SEQ ID NO:3 and wherein the polynucleotide with SEQ IFD NO:1 encoding a polypeptide with SEQ ID NO:3 works as a means for enhancing septation and fragmentation of the transformed bacterium and wherein the transformed bacterium is selected from a group which includes S.griseus. Thus Kawamoto et al. anticipate claims 1-15, 24-28 of this application as written. In response to the previous Office action, applicants have traversed the above rejection arguing that Kawamoto et al. does not anticipate claim 1 since Kawamoto et al. does not disclose each and every element of claim 1. Applicants specifically argue that Kawamoto et al. does not disclose providing a filamentous actinomycete bacterium lacking detectable endogenous SsgA as required to anticipate claim 1. Examiner respectfully disagrees with such an argument. This is because Kawamota et al. disclose a strain of Streptomyces NRRL B2682 which sporulates in liquid medium but produces profuse branches and does not sporulate in rich medium. Kawamoto et al. also disclose that the very same bacterium forms septum only after

transformation with ssgA. It is clear from this information that such a strain was not producing detectable levels of SsgA endogenously before transformation, because if detectable levels of SsgA was being produced by said strain, it would have formed septum and not spores or filaments. Even though the reference does not explicitly that the strain disclosed did not produce detectable levels of SsgA, Examiner takes the position that such a characteristic was inherent in that strain. Therefore, contrary to applicants argument, that Kawamoto et al. does disclose a filamentous actinomycete bacterium lacking detectable endogenous SsgA as required to anticipate claim 1. Since the Office does not have the facilities for examining and comparing applicants' argument that the prior art does not disclose a strain lacking endogenous SsgA, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the bacterial strain of the prior art does not possess the same material structural and functional characteristics of the claimed bacterial strain). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawamoto et al. as applied to claims 1, 3-9, 11, 13-15, 29-34 above, and further in view of the common knowledge in the art for making recombinant heterologous proteins. Claims 16-19 are drawn to

a method of making a heterologous protein using the filamentous bacterium produced by the method of claims 1, 3-9, 11, 13-15, 29-34. The method of making heterologous recombinant proteins by transforming host cells is well known in the art of molecular biology. Therefore with a strain of filamentous bacterium which undergoes fragmentation thereby increasing its total cell number and in turn increasing the production of any proteins that it produces, it would have been obvious to one of ordinary skill in the art to use such a filamentous bacteria to produce a heterologous protein by transformation techniques. One of ordinary skill in the art would have been motivated to do so as filamentous bacteria which are generally easily cultivated on a larger scale to produce large amounts of heterologous protein now available in fragmented form would be much more amenable for large scale cultivation because it overcomes the problems of clumping of mycelial masses thus allowing better nutrient and oxygen transport resulting in more growth and production of the intended product. One of ordinary skill in the art would have a reasonable expectation of success since Kawamoto et al. provide the technique for making such fragmented bacteria and the art provides techniques for transformation of such cells to produce any heterologous polypeptide by transformation. Therefore the above claims would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

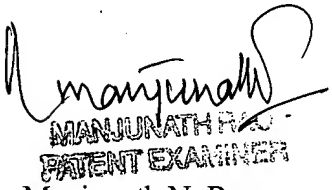
Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
August 1, 2003